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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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EXAMINER

ART UNIT	PAPER NUMBER
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DATE MAILED:

03/09/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 12-20-99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 46-64 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 46-64 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

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DETAILED ACTION

The request for the extension of time and appeal dated 10-20-99 and the filing under 1.129 (a) and amendment dated 12-20-99 are acknowledged.

Claims included in the prosecution are 46-64.

Claim Rejections - 35 U.S.C. § 112

- 1. The following is a quotation of the second paragraph of 35 U.S.C. 112:**

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

- 2. Claims 46-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

It is unclear what applicant intends to convey by 'stable liposome' in the independent claims. Stable is a relative term and stability of liposomes depends on the conditions to which they are exposed; such as time, light, temperature, oxidants etc. Without these parameters, the term has no meaning.

What is being conveyed by 'hydrophobic ions' in claim 54. The very fact that the drug is ionic means it will interact with either hydrogen ions or hydroxyl ions in water. If the drug is anionic in nature it will interact with hydrogen ions or if it is cationic in nature

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it will interact with the hydroxyl group. The compound might be hydrophobic, but ions are not since they interact with the ions in water.

The distinction between para-amino salicylic acid and salicylic acid derivative in claim 60 is unclear. The first named compound is a derivative of salicylic acid.

Claim Rejections - 35 U.S.C. § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 46-54, 56-57, and 61-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Nichols (BBA, 1976).

Nichols discloses disclosed a method of preparation of liposomes using instant method (note entire publication, page 270 in particular). The drugs loaded include epinephrine (page 271). The method involves preparing liposomes with acidic pH and titrating them with a base to create a pH gradient and adding a basic drug such as epinephrine to load the drug.

5. Claims 46-54, 57 and 61-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Deamer (BBA, 1972) of record.

Deamer discloses a method of preparation of liposomes using instant method (note entire publication, page 270 in particular). The compounds loaded include are amines (note

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abstract and Method section). The method involves preparing liposomes with acidic pH and titrating them with a base to create a pH gradient and adding a basic amine.

6. Claims 46-54, 59 and 61-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Cramer (BBRC, 1977) or Kano (BBA, 1978) already of record.

The references of Cramer and Kano disclose a method of loading substances using pH gradient (note the abstracts). The method involves the preparation of liposomes and lowering the pH of the external medium. The compounds loaded are acidic in nature (note the abstract and Materials and methods).

Claim Rejections - 35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 46-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols or Deamer or Cramer or Kano cited above.

Nichols and Deamer do not teach the establishment of the pH gradient by the addition of an acid. It is deemed however, to be within the skill of the art of chemistry that if the internal medium is basic one can only establish a gradient by the addition of a acidic substance (that is, altering the pH). Nichols does not teach instant drugs. However, Nichols

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and Deamer teach the concept of loading a chemical species into the liposomes using a pH gradient. It would have been obvious to one of ordinary skill in the art to load any drug with the expectation of similar loading since Nichols and Deamer teach the principle of loading.

Cramer and Kano do not teach the establishment of the pH gradient by the addition of a base. It is deemed however, to be within the skill of the art of chemistry that if the internal medium is acidic one can only establish a gradient by the addition of a basic substance (that is, altering the pH). Cramer and Kano do not teach instant drugs. However, Cramer and Kano teach the concept of loading a chemical species into the liposomes using a pH gradient. It would have been obvious to one of ordinary skill in the art to load any drug with the expectation of similar loading since both references teach the principle of loading.

Applicant's arguments based on the interference proceedings of the parent case have been fully considered, but are not found to be persuasive. Applicant's arguments in essence are based on a single term 'stable'. The examiner is not persuaded that this term makes a difference over the prior art's teachings since as pointed out above, this term is a relative term.

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.



Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

March 8, 2000